FOR RELEASE UPON DELIVERY

STATEMENT OF

HAROLD VARMUS, M. D.

DIRECTOR

NATIONAL INSTITUTES OF HEALTH

BEFORE THE

SENATE APPROPRIATIONS SUBCOMMITTEE

ON

LABOR, HEALTH AND HUMAN SERVICES, EDUCATION AND

RELATED AGENCIES

JANUARY 26, 1999

Mr. Chairman and Members of the Subcommittee:

I would like to thank you for the opportunity to discuss the recent decision by the Department of Health and Human Services concerning HHS funding for research utilizing human pluripotent stem cells. In testimony to this Subcommittee on December 2, 1998, I presented the exciting science of human pluripotent stem cells and described how the isolation of these cells could radically change the landscape of biomedical research. At that time, the NIH was awaiting a legal opinion from DHHS to determine whether or not the NIH could fund research utilizing these cells. The legal opinion is now available and states that research utilizing human pluripotent stem cells can be supported with Federal funds. What then are the next steps?

First, let me say that we understand and respect the different points of view that have been expressed about the important ethical and moral issues involved in this research. In developing the important safeguards that will govern funding for this research, NIH intends to consult with those representative of a broad range of views. We welcome the input of Congress as we move forward in this area.

Today, I would like to very briefly review some features of human pluripotent stem cells--how they are derived and the promises they hold for medical research and practice. I will then describe the legal opinion and the plans for the development of guidelines and oversight that will be in place before NIH would fund research with these cells. We are committed to proceeding in a careful and deliberate manner that recognizes the ethical, societal, and scientific issues of this area of research.

I refer you to my previous testimony for a fuller description of the scientific aspects of this research. Stem cells are cells that have the ability to reproduce themselves and to give rise to other more specialized types of cells. Totipotent stem cells--such as the product of fertilization of an ovum and its progeny--are stem cells that have total potency, which means that they have the ability to form an entire mature organism, e.g., a human being, although only if placed in a woman's uterus. In contrast, human pluripotent stem cells, which are under discussion today, do not have total potency, and hence cannot form an entire organism under any known condition. But pluripotent stem cells can give rise to all of the different types of specialized cells in the body.

The methodologies for deriving human pluripotent stem cells are not really new; pluripotent stem cells have been derived from mice since the early 1980s and, since then, from non-human primates and other animals. The first reports of deriving human pluripotent stem cells were published in November 1998 by Dr. John Gearhart and Dr. James Thomson. Neither of these investigations were supported with DHHS funds, although Dr. Gearhart's work could have been supported with Federal funds, because he and his colleagues derived human pluripotent stem cells from primordial gonadal tissue which was taken from a non-living fetus. Federal laws and regulations already exist that govern research on fetal tissue. Dr. Thomson and his co-workers derived pluripotent stem cells from the blastocyst stage of an early embryo--the embryos used were donated by couples who were receiving infertility treatment; this derivation of stem cells from the embryo does fall under the ban on Federal funding in the HHS/Labor/Education Appropriations Bill. The pluripotent stem cells derived by each of these means appear to be very similar or identical in structure, function, and potential; but it will take more research to verify

this.

The isolation and culturing of human pluripotent stem cells opens certain avenues of research for the first time. Let me mention just three potential applications of human pluripotent stem cells. The first is research focused on how stem cells differentiate into specific types of cells. The goal is to identify the genetic and environmental signals that direct the specialization of a stem cell to develop into specific cell types. Studying normal cell and tissue development will provide an understanding of abnormal growth and development which, in turn, could lead to the discovery of new ways to prevent and treat birth defects and even cancer.

A second and more practical application of research using these cells is in pharmaceutical development. Use of human pluripotent stem cells could allow researchers to study the beneficial and toxic effects of candidate drugs in many different cell types and potentially reduce the numbers of animal studies and human clinical trials required for drug development.

The third and most obvious potential application of these human pluripotent stem cells is to direct the specialization of the cells into cells and tissues that could be transplanted into patients for the purpose of repairing injury and pathological processes. A number of such examples are described in my December testimony, but two are worth mentioning here.

(i) Transplantation of healthy heart muscle cells could provide new hope for patients with heart disease. The hope is to develop heart muscle cells from human pluripotent stem cells and then transplant them into the failing heart muscle in order to augment the function of the heart. Preliminary work in mice and other animals has demonstrated that healthy heart

muscle cells transplanted into the heart successfully repopulate the heart tissue and integrate with the host cells. These experiments show that this type of transplantation is feasible.

(ii) In many individuals with Type I diabetes, the production of insulin in the pancreas by specialized cells called islet beta cells is disrupted. There is evidence that transplantation of either the entire pancreas or isolated islet cells could mitigate the need for insulin injections. Islet cell lines derived from human pluripotent stem cells could be used for this critical research and, ultimately, for transplantation.

Because human pluripotent stem cells continue to replicate robustly, stem cells derived from a few embryos or from a few fetuses could potentially be used in hundreds of individual research protocols.

Briefly, that is the science and the promise. We are here today to discuss the role of the Federal Government in the future of this area of research.

There are a number of advantages to using public funding for research. Perhaps the most important reason is the fact that Federal involvement creates a more open research environment--with better exchange of ideas and data among scientists--more public engagement and more oversight. In addition, Federal support increases the fiscal resources and expands the pool of talented investigators – particularly in academia – both of which accelerate the tempo of scientific discovery.

In response to the recent announcements concerning the isolation of human pluripotent stem

cells, I requested an opinion from DHHS on the legality of using DHHS funds to support or conduct research that utilizes these cells, in light of existing restrictions on human fetal tissue research and the amendment in our Appropriations bill governing human embryo research.

On January 15, 1999, DHHS delivered the following opinion. DHHS funds can be used to support research utilizing human pluripotent stem cells that are derived from human embryos: the statutory prohibition on human embryo research does not apply to research utilizing human pluripotent stem cells because human pluripotent stem cells are not embryos. The statute that bans the use of Federal funds for embryo research defines embryo as an organism derived by fertilization and other means. The statute does not, however, define organism. Therefore, the legal opinion relied on the broadly accepted science-based definition of organism: an individual constituted to carry out all life functions. By this definition--and as you heard from all the witnesses that responded to that question at your hearing on this matter on December 2, 1999--pluripotent stem cells are not and cannot develop into organisms. Therefore, human pluripotent stem cells are not embryos and are not covered by this prohibition on Federal funding. In addition, the legal opinion states that DHHS funds can be used for research using human pluripotent stem cells that were derived from fetal tissue if the existing laws and regulations governing fetal tissue research are obeyed.

Now that the legal opinion has been rendered, what are the next steps? The approach will be careful and deliberative, recognizing the important ethical concerns that surround this area of research. I want to emphasize that NIH will not use Federal funds for research using human pluripotent stem cells until guidelines and procedures to oversee the research are developed. Let me describe the process that we have planned to ensure that any research involving human

pluripotent stem cells is appropriately and carefully conducted. And as I mentioned earlier, we are interested in hearing a broad range of views.

First, all researchers currently receiving NIH support have been notified, via the NIH web site, that they cannot use DHHS funds to begin research using human pluripotent stem cells until further notice. We have made every effort to include this policy in all of our public statements. In addition, NIH program staff have been requested to notify those grantees who are most likely to have an interest in this work about this present policy. The Deputy Director for Intramural Research has also notified intramural scientists of these requirements.

Second, I will convene a subcommittee of the Advisory Committee to the Director (ACD) to develop Guidelines that specify what work using these cells can and cannot be supported with DHHS funds and outline restrictions on the use of such funds in the derivation of the cells. They will also be asked to develop an oversight mechanism to review research proposals seeking to conduct research utilizing these pluripotent stem cells. The subcommittee will meet in public session and will be composed of scientists, the lay public, ethicists, and lawyers; former members of the Human Embryo Research Panel may be asked to participate. They will be asked to consider advice from the National Bioethics Advisory Commission (NBAC), the newly established Council of Public Representatives (COPR), the public, and the Congress. NIH already has two thoughtful sets of Guidelines which will inform these efforts--the 1994 Report of the Human Embryo Research Panel and the regulations regarding Research on Transplantation of Fetal Tissue (section 498A of the Public Health Services Act). Once developed, Guidelines for research utilizing human pluripotent stem cells will be published in the Federal Register for public comment. We hope the Guidelines and oversight process will be operational within the

next several months.

In conclusion, the promise of human pluripotent stem cell research is great. And we are committed to addressing important issues surrounding this research in a deliberative and careful process to ensure that this research is conducted in an ethical, scientifically valid, and legal manner.

This concludes my statement. I would be pleased to respond to any questions you may have.